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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/408,396 09/29/99 BUHR

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HM12/1106

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EXAMINER

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OWENS JR, H

ART UNIT

PAPER NUMBER

1623

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DATE MAILED:

11/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/408,396

Applicant(s)

BUHR ET AL.

Examiner

Howard V Owens

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-8 is/are allowed.
- 6) ☒ Claim(s) 9-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>8</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1623

Reissue Application

Objections

The objection of this application under 37 CFR 1.172(a) as lacking the written consent of all assignees owning an undivided interest in the patent is withdrawn.

Oath/Declaration

The declaration filed with this application remains defective under 37 CFR 1.175. The declaration contains the statement that the errors arose without any deceptive intention on the part of the applicant. Applicants are not required under 37 CFR 1.175 to specify the details as to how the error arose or occurred; however, 37 CFR requires that the applicant particularly specify the defects and distinctly specify the excess or insufficiency in the claims. In the case of the instant claims applicants have stated that "patentees erred in not claiming the chemical compounds set forth in claims 9-26"; however, this statement is not accompanied by a rationale stating how not claiming the compounds is an error.

Specification

The objection to the specification for supplying a cut up copy has been overcome through applicant's submission of cut - up soft copies of the original patent.

Page 4, line 28 of the specification appears to contain either a missing period or parenthesis. Correction is required for this and any other grammatical or spelling errors not noted herein.

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35 U.S.C. 112(2)

The rejection of claims 9-19 under 35 U.S.C. 112, second paragraph, has been overcome through applicant's amendment.

35 U.S.C. 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gait, *Oligonucleotide Synthesis: A practical approach*, October 1984, in combination with Montgomery et al., *Journal of Medicinal Chem.*, vol.29 (11), 1986 and Perlman, J. of *Med. Chem.*, vol. 28, 1985, Greene et al., *Protective Groups in Organic Chemistry*, pp. 413-416, 1991.

In claims 9-19, a 2-Deoxy-2-fluoro- β -D-arabinofuranosyl with either a protected purine or pyrimidine is set forth. The compounds differ only through the protected exocyclic amines or the ether groups of the analog. The protecting agents used for the purines are benzoyl for adenine and cytosine and isobutyryl for guanine. The protecting group used for the ethers is 4,4-dimethoxytrityl.

Montgomery sets forth the analogous 2-Deoxy-2-fluoro- β -D-arabinofuranosyl compound set forth in claims 9-19 when the base is a purine (p. 2390). Perlman sets forth the analogous 2-Deoxy-2-fluoro- β -D-arabinofuranosyl compound set forth in claims 9-19 when the base is a pyrimidine (p.743). However, neither Montgomery nor Perlman teach the compound with the appropriate protecting groups for the exocyclic amine or ether

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moieties. Both Gait and Greene provide the nexus between applicant's invention and the prior art as it teaches the protection of exocyclic amino groups of heterocyclic bases via the use of the protecting group benzoyl for adenine and cytosine, and isobutyryl for guanine in oligonucleotide synthesis. Gait also teaches the use of dimethoxytrityl protecting groups for the temporary protection of the 5' hydroxyl group or an ether moiety during oligonucleotide synthesis (p. 12, paragraph 1 and p. 23, paragraph 1). Greene et al. teach the use of t-butyldimethylsilyl (TBMS) as a protecting agent for 5' hydroxyl groups/ethers.

It would have been prima facie obvious to use protecting groups for exocyclic amines and ethers in a purine or pyrimidine substituted 2-Deoxy-2-fluoro- β -D-arabinofuranosyl analog known in the prior art. .

One of skill in the art would have been motivated to use known protecting agents such as benzoyl, isobutyryl and dimethoxytrityl agents for exocyclic amines of heterocyclic bases or ether moieties given the use of these protecting agents for said moieties in oligonucleotide synthesis.

The rejection of claims 20-26 under 35 U.S.C. § 103 as being unpatentable over Gait, *Oligonucleotide Synthesis: A practical approach*, October, 1984 in combination with Sterzycki et al., EP 0316017 A2 is maintained for the reasons of record.

Claims 20-26 are drawn to a modified oligonucleotide or derivative thereof comprising at least one nucleoside selected from the group consisting of a 2'-deoxy-2'-fluoro-ribonucleoside, an arabinonucleoside, a 2'-deoxy-arabinonucleoside and a 2'-deoxy-2'-fluoro - arabinonucleoside.

Sterzycki et al. teach 2'-deoxy-2'-fluoro-arabinonucleosides and derivatives thereof (pp. 2 and 8-10). However, Sterzycki et al. does not teach the formation of oligonucleotide formation from the 2'-deoxy-2'fluoro-arabinonucleosides. The formation

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of oligonucleotides from nucleoside compounds is well known in the art. Gait teaches the synthesis of oligodeoxynucleotides from deoxyribonucleosides as well as the phosphorothiate and phosphoramidite internucleotide linkages.

It would have been *prima facie* obvious to synthesize an oligonucleotide from a modified 2'-deoxy-2'-fluoro-deoxyoligonucleotide or derivative thereof.

A person of ordinary skill in the art would have been motivated to produce the oligonucleotides from deoxynucleosides of the instant claims for the art recognized benefit of the construction, selection and determination of the DNA sequence of recombinants or site directed mutagenesis.

Applicant has broadly set forth classes of nucleoside compounds which as instantly claimed do not particularly denote novel compounds. Moreover, given the state of the art with regards to the synthesis of oligonucleotides, one of skill in the art would have a reasonable expectation of success in the formation of oligonucleotides from the broad classes of compounds set forth in the instant claims.

Applicant argues that the claims cannot be found obvious in view of prior art references unless the references themselves suggest that their respective teachings should be modified in a way that would produce the claimed invention; moreover that the motivation provided by the examiner is "simply not credible". Applicant's assertions do not serve as fact. Other than the statement that "site directed mutagenesis requires a naturally occurring nucleic acid", applicant provides no factual data to support this assertion. One of skill in the art would recognize that synthetic oligonucleotides are also required to alter genes through site directed mutagenesis. Moreover, the reference which has provided the motivation to form the oligonucleotide, Sproat et al., is the same reference applicant uses to form the oligonucleotide, thus applicant is questioning the credibility of the same reference it relies upon to make the claimed oligonucleotides. Assuming *arguendo* that one of skill in the art would not have had the same motivation as

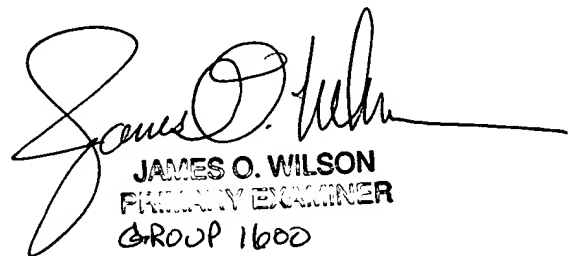
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the examiner, applicant's specification clearly points out that the state of the art has already provided a motivation for the formation of oligonucleotides from 2'deoxy-2'fluoro-ribonucleotides, p. 4, Ikehara, *Heterocycles*, specifically that these oligonucleotides have a higher affinity to DNA than normal oligodeoxyribonucleotides.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mr. Howard Owens whose telephone number is (703) 306-4538. The examiner can normally be reached on Tuesday-Friday 9 a.m.-6:30 p.m. (EST). The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.



JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600